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(54) Title: IMPROVED ORAL COMPOSITIONS FOR CONTROL AND PREVENTION OF TARTAR, ORAL MALODOR, PLAQUE AND GINGIVITIS

(57) Abstract

An oral composition that includes thymol, a zinc salt and a sweetener is disclosed. The oral composition has antitartar, antiplaque, antigingivitis efficacy, long lasting breath freshening and high consumer acceptability in spite of the presence of two ingredients, thymol and a zinc salt, that are known to taste bad.

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IMPROVED ORAL COMPOSITIONS FOR CONTROL AND PREVENTION OF TARTAR, ORAL MALODOR, PLAQUE AND GINGIVITIS

BACKGROUND OF THE INVENTION

1. Field of the Invention

This invention relates to oral compositions for treating and/or preventing diseases of the mouth, and more particularly to oral compositions for treating and/or preventing tartar, oral malodor, plaque and gingivitis. More specifically, this invention is directed to the use of zinc and essential oils in a mouthwash that has long lasting breath freshening, inhibits tartar and is effective against the microbes that cause plaque and gingivitis.

2. Description of Related Art

Thymol is a well known essential oil that has been used in mouthwash for many years for its antimicrobial properties. Thymol is one ingredient in Listerine® brand mouthwash. However, thymol is also well known for its very unpleasant, harsh taste. U.S. Patent No. 4,945,087 provides one solution to thymol's taste problem by masking the taste with a combination of sugar alcohol and anethole.

Zinc salts have been used over the years in several oral care products, primarily to limit or prevent malodor. Examples of such oral care products include AIM® toothpaste, Breath Savers® mints, Lavoris® mouthwash, Viadent® mouthrinse, and Listermint®.

The literature in this field shows there are numerous reasons to add zinc salts to oral care products. Among those reasons are its efficacy as an anti-malodor agent. Two mechanisms of action are believed to be responsible for zinc's utility as an anti-malodor agent. The first is its ability to form insoluble salts with nucleophilic compounds such as valeric acid, hydrogen sulfide, mercaptans, etc., (i.e. volatile sulfur compounds, "VSCs"), which typically cause oral malodor. U.S. Patent No. 4,992,259; Pader, M, Oral Hygiene Products and Practice, Chapter 10, pg. 351. Additionally, the literature shows that zinc salts inhibit proteolysis by direct action on bacterial proteases, like cysteine and

methionine proteases, thus reducing the amount of odor causing agents. Marsh, PD, J. Clin. Periodontal, 18(6): 462-467, 1991.

Zinc has also been shown to have antimicrobial efficacy. Here, its mode of action is believed to result from surfactant charge activity, resulting in disruption of membranes. Verran, J. Int. J. Cosmet. Sci., 13: 29-42, 1991. Zinc is also believed to inhibit essential enzymes in glucose transport and catabolism. Cummins D. J. Clin. Periodontol, 18: 455-461, 1991; and Marsh, PD, J. Clin. Periodontal, 18(6); 462-467, 1991.

Antiplaque and antigingivitis efficacy is another attribute of zinc salts. Part of this activity may be a direct consequence of its antimicrobial efficacy. Further, zinc may reduce the rate of bacterial adherence to teeth. Harrap, GJ, Saxton, CA, Best, JS, Archs.Oral. Bio., 29(2): 87-91, 1984; and Harrap, GJ, Saxton, CA, Best, JS, J. Periodont Res., 18: 634-642, 1983. Zinc is also said to prevent the toxic effects that volatile sulfur compounds have on membrane permeability by preventing VSC penetration into epithelial cells. Pader, M, Oral Hygiene Products and Practice, Chapter 10, pg. 351-352.

Moreover, zinc has been associated with anticaries activity resulting from inhibition of the dissolutive process of caries by reversible adsorption on apatite. Ingram, GS, Edgar, WM, Adv. Dent. Res., 8(2): 158-65, 1994.

Finally, zinc salts are believed to also have anticalculus efficacy resulting from adsorption of zinc ion on apatite, thus restricting crystal growth. Ingram, GS, Edgar, WM, Adv. Dent. Res., 8(2): 158-65, 1994; Ingram, GS, Horay, CP, Stead, WJ, Caries, Res., 26(4): 248-253, 1992 and Gilbert, RJ, Ingram, GS, J. Pharm. Pharmacol., 40(6): 399-402, 1988.

Use of zinc salts in oral compositions has several drawbacks, however. An unpleasant aftertaste frequently occurs, which is often characterized as metallic or astringent. Such unpleasant aftertaste limits consumer acceptance of oral care products containing zinc.

U.S. Patent No. 4,022,880 to Vinson et al. teaches oral compositions including mouthwash that retard the development of dental calculus that contain 0.05% to about 4% zinc ions.

U.S. Patent No. 5,095,035 to Eby teaches zinc acetate containing oral products to which saccharin is added as a super sweetener.

Listerine® brand mouthwash has been sold in the United States for approximately 100 years. Listerine® contains thymol, menthol, eucalyptol and methyl salycilate.

SUMMARY OF THE INVENTION

The present invention is directed to mouthwash compositions that contain zinc salts and thymol that provide antitartar, antiplaque, antigingivitis efficacy and long lasting breath freshening, yet have high consumer acceptability in spite of the presence of two ingredients, thymol and a zinc salt, that are known to taste bad.

More particularly, the present invention is directed to a mouthwash composition comprising thymol and a zinc salt in combination with a sweetener.

BRIEF DESCRIPTION OF THE DRAWINGS

Fig. 1. is a graph of the induction time for precipitation of hydroxyapatite vs. percent zinc chloride in both mouthwash and aqueous solution using 3.0 ml of sample.

Fig. 2. is a graph of the induction time for precipitation of hydroxyapatite vs. percent zinc chloride in both mouthwash and aqueous solution using 1.5 ml of sample.

Fig. 3. is a graph of the induction time for precipitation of hydroxyapatite vs. percent zinc acetate in aqueous solution using 1.5 ml of sample.

Fig. 4. is a photograph (at 29x) of a crystal of dicalcium phosphate dihydrate (DCPD).

Fig. 5. is a photograph (at 29x) of a crystal of DCPD formed in the presence of 0.01% Zn.

Fig. 6. is a photograph (at 29x) of a crystal of DCPD formed in the presence of 0.09% Zn.

Fig. 7. is a photograph (at 29x) of a crystal of DCPD formed in the presence of 0.15% Zn.

Fig. 8. is a photograph (at 29x) of a crystal of DCPD formed in the presence of 0.20% Zn.

Fig. 9. is a photograph (at 29x) of a crystal of DCPD formed in the presence of 0.40% Zn.

Fig. 10 is a graph showing the effect on a cysteine VSC response of rinsing with a mouthwash without zinc.

Fig. 11 is a graph showing the effect on the cysteine VSC response of rinsing with mouthwash with 0.1% $ZnCl_2$.

Fig. 12 is a graph showing the effect on the cysteine VSC response of rinsing with mouthwash with 0.21% zinc sulfate.

Fig. 13 is a graph showing the effect on the cysteine VSC response of rinsing with Viadent®, which contains 0.2% $ZnCl_2$.

DETAILED DESCRIPTION OF THE INVENTION

The oral compositions of this invention contain thymol. The thymol is usually present in amounts of not more than about 0.1% by weight, based on the weight of the total composition, with about 0.02 to about 0.1% by weight being preferred, and about 0.05 to about 0.075% by weight being most preferred.

Suitable zinc salts for use in the present invention are well known in the art, and are those which freely ionize in an aqueous or hydroalcohol base. Suitable salts include inorganic, organic and water insoluble and water soluble zinc salts. Nonlimiting examples of suitable zinc salts that may be employed include:

zinc oxide
Zinc tribromosalicylanilide
Zinc carbonate
Zinc caprylate
Zinc oleate
Zinc silicate
Zinc acetate
Zinc lactate
Zinc fumarate
Zinc ammonium sulfate
Zinc bromide
Zinc chloride
Zinc chromate
Zinc citrate
Zinc dithionate
Zinc fluorosilicate
Zinc tartarate
zinc stearate
zinc methionine sulfate
zinc tannate
zinc octoate
zinc laurate
zinc fluoride
zinc formate
zinc succinate
zinc iodide
zinc nitrate
zinc phenol sulfonate
zinc salicylate
zinc sulfate
zinc gluconate
zinc succinate
zinc glycerophosphate

Preferred salts are zinc chloride, zinc citrate, zinc oxide, zinc acetate, zinc stearate, zinc methionine sulfate, zinc phenol sulfonate, zinc sulfate, and zinc gluconate. The most preferred salts are zinc chloride, zinc sulfate, and zinc citrate.

The zinc salt is added to the composition in an amount sufficient to provide zinc ions in amount from about 0.005 to about 0.095 % w/v of the composition. Preferably the amount of zinc salt added to the composition is sufficient to provide zinc ions in an amount from about 0.02 to about 0.09 % w/v of the composition. More preferably, the amount of zinc salt added to the composition is sufficient to provide zinc ions in an amount from about 0.03 to about 0.085 % w/v of the composition. Even more preferably, the amount of zinc salt added to the composition is sufficient to provide zinc ions in an amount from about 0.03 to about 0.043 % w/v of the composition. Additionally, the amount of zinc ions can be from about 0.045 to about 0.075% w/v of the composition.

The compositions of this invention may, in addition to the thymol and zinc salt, include effective amounts of other essential oils such as those selected from the group consisting of eucalyptol, menthol, methyl salicylate, and the like, and mixtures thereof. Generally, the total amount of essential oils present in a composition, exclusive of the thymol, can be from about 0.05 to about 0.35% by weight, based on the weight of the composition, with about 0.12 to about 0.28% by weight being preferred. For example, the compositions, as stated above, can contain eucalyptol, menthol, and methyl salicylate. Preferably the eucalyptol is present in amounts of about 0.07 to about 0.11% being preferred and most preferably about 0.08 to about 0.10%; preferably menthol is present in amounts of about 0.03% to about 0.06% by weight and most preferably about 0.04 to about 0.05%; and preferably methyl salicylate is present in amounts of about 0.03 to about 0.08% by weight and most preferably about 0.04 to about 0.07%. All of the percent amounts of essential oils are of the total composition.

The compositions of the present invention include liquid oral preparations such as a mouthwash, spray or rinse. In such preparations the vehicle --i.e. the carrier for the ingredients of the mouthwash, such as the essential oils, and the like-- is typically a water-alcohol mixture. However, as disclosed in U.S. Patent No. 5,723,106, reduced alcohol mouthwashes can be formulated with same taste properties as higher alcohol

mouthwashes. Additionally, it is known the mouthwashes with no alcohol can be made with the same or similar properties as alcohol containing mouthwashes. The oral compositions according to the present invention include reduced alcohol and no alcohol mouthwashes.

If alcohol is present, the ratio of water to alcohol is in the range of from about 1:1 to about 20:1, preferably about 3:1 to about 20:1 and most preferably about 3:1 to about 10:1 by weight. The total amount of water-alcohol mixture in a mouthwash preparation is typically in the range from about 50% to about 99.9% by weight of the composition. The pH value of such mouthwash preparations is generally from about 3.5 to about 8.0 and preferably from about 4 to about 6.0. A pH below 3.5 would be irritating to the oral cavity and soften tooth enamel. A pH greater than 8 would result in an unpleasant mouth feel.

The oral compositions according to the present invention may also contain surface active agents --i.e. surfactants-- in amounts up to about 5%. Surface active agents (surfactants) are organic materials that aid in the complete dispersion of the preparation throughout the oral cavity. The organic surface active material may be anionic, non-ionic, ampholytic, or cationic. Suitable anionic surfactants are water-soluble salts of higher fatty acid monoglyceride monosulfates, such as the sodium salt of the monosulfated monoglyceride of hydrogenated coconut oil fatty acids; higher alkyl sulfates, such as sodium lauryl sulfate; alkyl aryl sulfonates, such as sodium dodecyl benzene sulfonate; higher alkyl sulfonacetates; higher fatty acid esters of 1,2-dihydroxy propane sulfonates; and substantially saturated higher aliphatic acyl amides of lower aliphatic amino carboxylic acids such as those having 12 to 16 carbons at the fatty acid, alkyl or acyl radicals. Examples of the last mentioned amides are N-lauroyl sarcosine, and the sodium, potassium, and ethanolamide salts of N-lauroyl, N-myristyl or N-palmitoyl sarcosine.

The non-ionic surfactants employed are poly(oxyethylene)-poly(oxypropylene) block copolymers. Such copolymers are known commercially as poloxamers and are produced in a wide range of structures and molecular weights with varying contents of ethylene oxide and propylene oxide. The non-ionic poloxamers according to the invention are non-toxic and acceptable as direct food additives. They are stable and

readily dispersible in aqueous systems and are compatible with a wide variety of formulating ingredients for oral preparations. These surfactants should have an HLB (Hydrophilic-Lipophilic Balance) of between about 10 and 30 and preferably between 10 and 25.

Thus, non-ionic surfactants useful in this invention include poloxamers. Generally these polymers should constitute from 0.1% to 2% by weight of total volume of liquid oral preparation (% w/v) and preferably from 0.2% to 1% w/v. A particularly preferred poloxamer is Poloxamer 407 having an HLB of about 18-23. Such a polymer is sold under the trademark Pluronic F-127 (BASF-WYANDOTTE). The molecular weight distribution of Poloxamer 407 is reported to be approximately 11,800-12,600.

Another class of non-ionic surfactants useful in this invention are ethoxylated hydrogenated castor oils. Such surfactants are prepared by hydrogenating castor oil and treating the so-formed product with from about 10 to 200 moles of ethylene glycol. They are designated as PEG (numeral) hydrogenated castor oil in accordance with the dictionary of the Cosmetics, Toiletries and Fragrance Association, 3rd Ed. wherein the numeral following PEG indicates the degree of ethoxylation, i.e. the number of moles of ethylene oxide added. Suitable PEG hydrogenated castor oils include PEG 16, 20, 25, 30, 40, 50, 60, 80, 100 and 200. The ethoxylated hydrogenated castor oils are used in the same concentrations as the above described poly(oxyethylene)-poly(oxypropylene) block co-polymers.

Other non-ionic surface active agents that may be suitable include condensates of sorbitan esters of fatty acids with from 20 to 60 moles of ethylene oxide (e.g., "Tweens" a trademark of ICI United States, Inc.), and amphoteric agents such as quaternized imidazole derivatives.

Additional non-ionic surfactants that may be suitable are the condensation products of an alpha-olefin oxide containing 10 to 20 carbon atoms, a polyhydric alcohol containing 2 to 10 carbons and 2 to 6 hydroxyl groups and either ethylene oxide or a heteric mixture of ethylene oxide and propylene oxide. The resultant surfactants are polymers having a molecular weight in the range of 400 to about 1600 and containing 40% to 80% by weight of ethylene oxide, with an alpha-olefin oxide to polyhydric alcohol mole ratio in the range of about 1:1 to 1:3.

Cationic surface active agents that may be suitable are molecules that carry a positive charge such as cetylpyridinium chloride, domiphen bromide, benzylkonium chloride, and dequalinium chloride.

Fluorine providing compounds may be present in the oral preparations of this invention. These compounds may be slightly water soluble or may be fully water soluble and are characterized by their ability to release fluoride ions or fluoride containing ions in water. Typical fluorine providing compounds are inorganic fluoride salts such as soluble alkali metal, alkaline earth metal, and heavy metal salts, for example, sodium fluoride, potassium fluoride, ammonium fluoride, cuprous fluoride, zinc fluoride, stannic fluoride, stannous fluoride, barium fluoride, sodium fluorosilicate, ammonium fluorosilicate, sodium fluorozirconate, sodium monofluorophosphate, aluminum mono- and difluorophosphate and fluorinated sodium calcium pyrophosphate.

Alkali metal, tin fluoride and monofluorophosphates such as sodium and stannous fluoride, sodium monofluorophosphate and mixtures thereof are preferred.

In an oral liquid preparation such as a mouthwash, the fluorine providing compound is generally present in an amount sufficient to release up to about 0.15%, preferably about 0.001% to about 0.1% and most preferably from about 0.001% to about 0.05% fluoride by weight of the preparation.

The present invention also includes a high intensity sweetener. The sweetener is used is small amounts but is present in amounts sufficient to make the composition acceptable to most consumers in spite of the presence of two ingredients, thymol and a zinc salt, that are known to taste unpleasant. The high intensity sweeteners useful in the compositions of the present invention include water-soluble artificial sweeteners such as the soluble saccharin salts, i.e. sodium or calcium saccharin salts, cyclamate salts, the sodium, ammonium or calcium salt of 3,4-dihydro-6-methyl-1,2,3-oxathiazine-4-one-2,2-dioxide, the potassium salt of 3,4-dihydro-6-methyl-1,2,3-oxathiazine-4-one-2,2-dioxide (acesulfame-K), the free acid form of saccharin, dipeptide based sweeteners, such as L-aspartic acid derived sweeteners, such as L-aspartyl-L-phenylalanine methyl ester (aspartame), sucralose, xylitol and materials described in U.S. Pat. No. 3,492,131, L-aspartyl-N-(2,2,4,4--tetramethyl-3-thietanyl)-D-alaninamide hydrate, methyl esters of

L-aspartyl-L-phenylglycerine and L-aspartyl-L-2,5,dihydrophenyl-glycine, L-aspartyl-2,5-dihydro-L-phenylalanine; L-aspartyl-L-(1-cyclohexyen)-alanine; and the like.

The amount of sweetener needed in composition is dependent on the sweetening profile of the particular sweetener. The amounts can be readily determined by those skilled in the art.

A preferred high intensity sweetener is saccharin. The saccharin can be added in granular or spray dried form. The amount of saccharin useful in the compositions of the present invention is from about 0.001 to about 0.25 percent by weight of the composition, preferably from about 0.01 to about 0.2 percent by weight of the composition and even more preferably from about 0.05 to about 0.15 percent by weight of the composition.

In addition to the sweeteners described above, auxiliary sweeteners may be utilized in the compositions of this invention. Suitable natural and artificial sweeteners are known in the art. The sweetening agent (sweetener) used may be selected from a wide range of materials including water-soluble sweetening agents, water-soluble artificial sweeteners, water-soluble sweetening agents derived from naturally occurring water-soluble sweeteners and mixtures thereof. Without being limited to particular sweeteners, representative illustrations include monosaccharides, disaccharides and polysaccharides such as xylose, ribose, glucose (dextrose), mannose, galactose, fructose (levulose), sucrose (sugar), maltose, invert sugar (a mixture of fructose and glucose derived from sucrose), partially hydrolyzed starch, corn syrup solids, dihydrochalcones, monellin, steviosides, and glycyrrhizin; and protein based sweeteners such as thaumatoccous danielli (Thaumatin I and II).

Additional flavorings (flavors) may be added. The flavorings (flavoring agents) that may be used include those known to the skilled artisan, such as, natural and artificial flavors. These flavorings may be chosen from synthetic flavor oils and flavoring aromatics, and/or oils, oleo resins and extracts derived from plants, leaves, flowers, fruits and so forth, and combinations thereof. Representative flavor oils include: spearmint oil, cinnamon oil, oil of wintergreen (methyl salicylate), peppermint oil, clove oil, bay oil, eucalyptus oil, thyme oil, cedar leaf oil, oil of nutmeg, oil of sage, and oil of bitter almonds. Also useful are artificial, natural or synthetic fruit flavors such as vanilla, and

citrus oil, including lemon, orange, grape, lime and grapefruit and fruit essences including apple, pear, peach, strawberry, raspberry, cherry, plum, pineapple, apricot and so forth. These flavorings may be used individually or in admixture. Commonly used flavors include mints such as peppermint, menthol, artificial vanilla, cinnamon derivatives, and various fruit flavors, whether employed individually or in admixture.

Flavorings such as aldehydes and esters including cinnamyl acetate, cinnamaldehyde, citral, diethylacetal, dihydrocarvyl acetate, eugenyl formate, p-methylanisole, and so forth may also be used. Generally any flavoring or food additive such as those described in Chemicals Used in Food Processing, pub 1274 by the National Academy of Sciences, pages 63-258 may be used.

Further examples of aldehyde flavorings include, but are not limited to acetaldehyde (apple); benzaldehyde (cherry, almond); cinnamic aldehyde (cinnamon); citral, i.e., alpha citral (lemon, lime); neral, i.e. beta citral (lemon, lime); decanal (orange, lemon); ethyl vanillin (vanilla, cream); heliotropine, i.e. piperonal (vanilla, cream); vanillin (vanilla, cream); alpha-amyl cinnamaldehyde (spicy fruity flavors); butyraldehyde (butter, cheese); valeraldehyde (butter, cheese); citronellal (modifies, many types); decanal (citrus fruits); aldehyde C-8 (citrus fruits); aldehyde C-9 (citrus fruits); aldehyde C-12 (citrus fruits); 2-ethyl butyraldehyde (berry fruits); hexenal, i.e. trans-2 (berry fruits); tolylaldehyde (cherry, almond); veratraldehyde (vanilla); 2,6-dimethyl-5-heptenal, i.e. melonal (melon); 2-6-dimethyloctanal (green fruit); and 2-dodecenal (citrus, mandarin); cherry; grape; mixtures thereof; and the like.

The amount of flavoring employed is normally a matter of preference subject to such factors as flavor type, individual flavor, and strength desired. Thus, the amount may be varied in order to obtain the result desired in the final product. Such variations are within the capabilities of those skilled in the art without the need for undue experimentation. In general, amounts of about 0.01% to about 2.0% by weight of the composition are useable with amounts of about 0.025% to about 1.5% being preferred.

The compositions of this invention may also contain coloring agents or colorants. The coloring agents are used in amounts effective to produce the desired color. The coloring agents (colorants) useful in the present invention, include the pigments such as titanium dioxide, which may be incorporated in amounts of up to about 2% by weight of

the composition, and preferably less than about 1% by weight. Colorants may also include natural food colors and dyes suitable for food, drug and cosmetic applications. These colorants are known as F.D. & C. dyes and lakes. The materials acceptable for the foregoing spectrum of use are preferably water-soluble, and include indigoid dye, known as F. D. & C. Blue No. 2, which is the disodium salt of 5,5-indigotindisulfonic acid. Similarly, the dye known as Green No. 1 comprises a triphenylmethane dye and is the monosodium salt of 4-[4-N-ethyl-p-sulfobenzylamino)diphenylmethylene]-[1-N-ethyl-N-p-sulfoniumbenzyl)-2,5 -cyclohexadienimine]. Additional examples include the yellow dye, known as D&C Yellow No. 10, the dye known as F.D.& C. Green No. 3 that comprises a triphenylmethane dye and the dye F.D. & C. Blue No. 1 that comprises the disodium salt of ethyl [4-[*p*[ethyl (*m*-sulfobenzyl)amino]-*a*-(*o*-sulfophenyl)benzylidene]-2,5-cyclohexadien-1-ylidene] (*m*-sulfobenzyl) ammonium hydroxide inner salt.. A full recitation of all F.D.& C. and D. & C. dyes and their corresponding chemical structures may be found in the Kirk-Othmer Encyclopedia of Chemical Technology, Volume 5, Pages 857-884, which text is accordingly incorporated herein by reference.

Additionally, the present invention may include a preservative in concentration ranges of from about 0.05% to about 2.0% by weight. Such preservatives include benzoic acid and sodium benzoate, among others. However, any pharmaceutically or orally acceptable preservative may be used to prepare the present invention. Sodium benzoate is typically present in amount of about 0.01-1% by weight, preferably about 0.025-0.8%.

The compositions according to the present invention can also include an alcohol having 3 to 6 carbon atoms. Preferred alcohols having 3 to 6 carbon atoms are aliphatic alcohols. A particularly preferred aliphatic alcohol having 3 carbons is 1-propanol. The amount of 3 to 6 carbon alcohol in the composition is from about 0.1 to about 1.5% by weight of the composition. A preferred amount of 3 to 6 carbon alcohol in the composition is from about 0.3 to about 1.0% by weight of the composition. A more preferred amount is from about 0.5 to about 0.75% by weight of the composition.

The following studies were performed to show that the claimed invention has anti-tartar efficacy, extended oral malodor protection and high consumer acceptability is spite of the presence of two ingredients that are known to taste bad.

ANTI-TARTAR STUDIES

A study was done to determine the anti-calculus effect of zinc salts in mouthwashes by determining the effect on the formation of calcium phosphate.

Human dental calculus consists of inorganic or mineral and organic phases. The mineral phase is composed of a mixture of calcium phosphates, namely, dicalcium phosphate dihydrate (DCPD), octacalcium phosphate (OCP), magnesium-substituted beta-tricalcium phosphate (β-TCMP) and carbonate hydroxyapatite (CHA). Several anti-calculus agents such as pyrophosphates, statherins, gantrez, magnesium salts and zinc salts have been proposed to retard the formation of calculus on tooth surfaces. These agents are usually compounds that inhibit the formation of calcium phosphate, mainly apatite.

In general, two tests have been used to evaluate the inhibitors. One test follows the spontaneous formation of apatite using a metastable or supersaturated calcium phosphate solution. "Inhibition" is related to the induction time or the time it takes the solution to spontaneously form apatite. Generally, in these tests, the anticalculus agent is added to the metastable solution. In the test for this study, Zn-containing solutions of zinc chloride and zinc acetate and zinc-containing mouthwash were used directly. Mouthwash samples containing different zinc concentrations, in weight per cent, were prepared. The formulas are summarized in Tables 1 and 2:

One liter of a stock solution was prepared as follows. All units, except as noted, are grams.

Alcohol U.S.P.	227 ml
Menthol	0.425
Thymol	0.639
Methyl salicylate	0.660
Eucalyptol	0.922
Mint Flavor	0.5
1-propanol	5.0
Poloxamer 407	2.5
Benzoic Acid	1.05
Sodium benzoate	0.53
Sodium saccharin	1.17
Granular	
Water	qs to 1000 ml

The stock solution was mixed and used to make three mouthwash compositions.

TABLE 1

	Formula 1	Formula 2	Formula 3
Stock Solution	333.3 ml	333.3 ml	333.3 ml
$ZnCl_2$	0.9	1.5	2
Sorbitol Solution	200	200	200
FD&C Blue No. 1	0.006	0.006	0.006
FD&C Red No. 40	0.0005	0.0005	0.0005
Water	qs to 1 ltr	qs to 1 ltr	qs to 1 ltr

The pH of the three formulas was adjusted with NaOH to 4.19 to 4.20.

Three additional formulas are summarized in Table 2.

TABLE 2

	FORMULA 4	FORMULA 5	FORMULA 6
ALCOHOL U.S.P.	227 ml	227 ml	227 ml
MENTHOL	.425	.425	.425
METHYL SALICYLATE	.660	.660	.660
EUCALYPTOL	.922	.922	.922
THYMOL	.639	.639	.639
MINT FLAVOR	.5	.25	.25
1-PROPANOL	5.0	5.0	5.0
BENZOIC ACID	1.05	1.05	1.05
SODIUM BENZOATE	.53	.53	.53
SODIUM SACCHARIN, GRANULAR	1.17	1.17	1.17
ZINC CHLORIDE	1.5	.9	.9
SORBITOL SOLUTION	200	200	200
FD&C BLUE NO. 1	.006	.006	.006
FD&C RED NO. 40	.0005	.0005	-
WATER	QS TO 1 LTR	QS TO 1 LTR	QS TO 1 LTR

Zinc chloride solutions at concentrations of 0.09, 0.15, and 0.20% were prepared. Zinc acetate solutions at concentrations of 0.0, 0.09, 0.15 and 0.20% were prepared.

A calcium phosphate metastable solution (CPMS) was prepared by mixing 20 ml of 0.225 M NaC1; 80 ml of 4.185 mM $CaC1_2$ and 50 ml, 2.805 mM Na_2HPO_4 in a 250 ml beaker. The solution was adjusted to pH 7.4.

A beaker containing the continuously stirred CPMS was immersed in a waterbath maintained at 37°C. This CPMS was prepared to give a one (1) minute induction time before the initial precipitation of calcium phosphate. The precipitation signals a Dosimat to add drops of a 0.012 M NaOH solution. Samples containing zinc ions were added to the CPMS (150 ml) in 1.5 and 3.0 ml volumes. The starting pH of the metastable solution after addition of the sample was recorded. Formation of calcium phosphate was indicated by the change in the pH and the observation of suspensions of microparticles

shown by Tyndall effect. Induction time was established as the time required for the initial precipitation to occur without (control) and with the addition of the zinc-containing samples. Measurements were made in duplicates or triplicates and results presented as the average values.

The results obtained with the mouthwash samples containing $ZnCl_2$ at various levels and using 1.5 and 3.0 ml samples are summarized in Table 3. The results obtained with the aqueous solutions containing $ZnCl_2$ at various levels and using 1.5 and 3.0 ml samples are summarized in Table 4. The results obtained with aqueous solutions containing ZnAc at various levels and using 1.5 ml samples are summarized in Table 5. In each of Tables 3-5, the original and actual concentration of zinc is reported. The original zinc concentration is the amount of zinc salt in the mouthwash or aqueous solution. The actual concentration of zinc is the amount of zinc after it is added to the 150 ml of CPMS.

The effect of zinc on induction time using $ZnCl_2$ with a 3.0 ml sample in both the mouthwash and aqueous solution is summarized in Fig. 1. The effect of zinc on induction time using $ZnCl_2$ with a 1.5 ml sample in both the mouthwash and aqueous solution is summarized in Fig. 2. The effect of zinc on induction time using ZnAC with a 1.5 ml sample in aqueous solution is summarized in Fig. 3.

When undiluted mouthwash was used, immediate cloudiness (indicating precipitation) was observed upon addition of NaOH. Infrared absorption analyses of precipitate from control showed the presence of apatitic calcium phosphate. The mouthwash sample with .2% Zn showed the presence of amorphous calcium phosphate.

The zinc chloride solutions were observed to have sediment at the bottom of the bottles. The higher the Zn concentration, the greater the amount of the sediment, due to high pH. At high pH, $ZnCl_2$ hydrolyzes to Zn $(OH)_2$ and ZnO.

The results obtained from the Zn solutions prepared from $ZnC1_2$, as shown in Fig. 1, may be due to the sediment, which is possibly reprecipitated $ZnC1_2$, and would then change the original zinc concentration. Results obtained from the Zn solutions prepared with ZnAc demonstrated a dose response, as shown in Fig. 3. The difference in results obtained from the $ZnC1_2$ solution compared to the mouthwash, at 0.15% $ZnCl_2$ using 1.5

ml of the solution, may be due to the buffer capacity and greater acidity of the mouthwash, causing the Zn^{2+} ions to stay in solution.

A difference in induction time is observed between metastable calcium phosphate solution CPMS (control) and the Zn-containing solutions. For example, time induction of 4 min observed for mouthwash or Zn acetate solutions indicate that such solution would take 4 time longer than the control before precipitation of apatitic calcium phosphate to appear.

The induction time observed for the mouthwash formulations containing 0.09% Zn - Formulas 1, 5 and 6 are almost identical and three times that of the control.

The formation of amorphous calcium phosphate (ACP) in the presence of Zn confirm studies reported previously that the presence of Zn disturbs the crystallization of apatite and promotes the formation of beta Zn-substituted tricalcium phosphate or BTCMP. Zn ions inhibit the formation of apatite and at slightly elevated concentration, promote the formation of ACP, which is more soluble than apatite.

Taken together, these results show that the optimum $ZnCl_2$ concentration for maximum efficiency of inhibiting or minimizing calcium phosphate, also known as apatitic formation, is from 0.09%. – 0.15% In the presence of zinc, the rate of formation of apatite, which is one of the calcium phosphate crystals in tartar, was significantly reduced. These results also suggest that adding zinc salt to a suitable oral compositions vehicle would be effective for inhibiting tartar formation.

TABLE 3: MOUTHWASH SAMPLES				
SAMPLE	% $ZnCl_2$ (ORIG)	% $ZnCl_2$ (ACTUAL)	pH AFTER *	INDUCTION TIME (MIN)
Control 1	0.0	0.0		1.0
Control 2	0.0	0.0		1.0
(A) Formula 1	0.09	0.0009	6.82	3.5
(B) Formula 2	0.15	0.0015	6.71	16
(C) Formula 3	0.20	0.0020	6.59	8.5
(D) Formula 4	0.15	0.0015	6.71	20.0
(E) Formula 5	0.09	0.0009	6.89	3.5
(AA) Formula 1	0.09	0.0018	6.68	8.5
(EE) Formula 5	0.09	0.0018	6.56	6.5
(BB) Formula 2	0.15	0.0030	6.52	7.0
(CC) Formula 4	0.20	0.0040	6.42	<1.0

[Volume of samples added, 1.5 ml for A, B. C, D, and E; 3.0 ml for AA, BB, CC, EE. * pH after adding sample to CPMS; pH of control, 7.4

TABLE 4: ZINC CHLORIDE SOLUTIONS			
% $ZnCl_2$ CONC (ORIG)	% $ZnCl_2$CONC (ACTUAL)	pH AFTER *	INDUCTION TIME (MIN)
0.09 (A)	0.0009	7.16	3.0
0.15 (B)	0.0015	7.01	5.5
0.20 (C)	0.0020	6.88	2.0
0.09 (AA)	0.0018	7.00	7.0
0.15 (BB)	0.0030	6.72	5.0
0.20 (CC)	0.0040	6.51	1.7

TABLE 5: ZINC ACETATE SOLUTION			
% $ZnAc_2$ CONC (ORIG)	% $ZnAc_2$ CONC (ACTUAL)	pH AFTER *	INDUCTION TIME (MIN)
0.09% (A)	0.0009	7.25	1.8
0.15(B)	0.0015	7.16	2.0
0.20 (C)	0.0020	7.05	3.5

[For all tables, the induction time reported was calculated as the average of 2 to 4 experiments. For Tables 2 and 3, 1.5 ml was used for samples A, B, C; 3.0 ml, for samples AA, BB, CC in Table 2; *pH after adding sample to CPMS].

Photographs Of Crystalline Dicalcium Phosphate

Photographs of crystalline dicalcium phosphate dihydrate were taken to show the effect of $ZnCl_2$ on the growth of the crystals. The crystals were prepared as follows. A 5% solution of sodium meta silicate, 9-hydrate is prepared. While stirring, sodium phosphate monobasic, monohydrate is added to make a 0.3M phosphate solution. The pH of the phosphate/silica solution is adjusted to 6.0 using acetic acid. Thirty mL of solution is poured into 25x150mm size test tubes and covered. The gel completely solidifies in 2-3 days at room temperature.

A 0.3M calcium acetate solution with the indicated amount of zinc chloride is prepared and the pH of the calcium/zinc solutions is adjusted to 4.2 using acetic acid. The zinc chloride solutions were prepared in the stock solution described above. Ten ml of the calcium/zinc solution is added to the top of the solidified gels. The tubes are incubated at 25 C. The photos of the dicalcium phosphate dihydrate (DCPD) crystals in the gels were taken with a Mamiya medium format camera, equipped with a 55mm lens.

Fig. 4 is a photograph of a crystal of dicalcium phosphate dihydrate (DCPD). Figs. 5-9 are photographs of crystals of dicalcium phosphate dihydrate formed in the presence of 0.01, 0.09, 0.15, 0.20 and 0.40% $ZnCl_2$, respectively. As the amount of zinc increases, the size and quantity of DCPD changes.

In Fig. 5 with 0.01% $ZnCl_2$, DCPD appears normal, showing the typical triangular plate habits when obtained from systems containing only calcium and phosphate ions. The size and appearance of DCPD is apparently not affected by 0.01% $ZnCl_2$.

In Fig. 6 with 0.09% $ZnCl_2$, the number of DCPD crystals is significantly decreased and a few roundish minute crystals of DCPD are also present. These spherical structures are most likely changed phases of DCPD.

In Fig. 7 with 0.15% $ZnCl_2$, DCPD is also decreased quantitatively. Appearance and number of crystals is similar to the effect observed with 0.09% zinc chloride.

In Fig. 8 with 0.20% $ZnCl_2$, DCPD remains unchanged. In addition, a row of "flower" like amorphous mass appears together with existing DCPD. These structures may be zinc substituted beta-TCMP.

In Fig. 9 with 0.40% $ZnCl_2$, the regular structure of DCPD is replaced by a significant amount of DCPD and perhaps zinc substituted beta TCMP.

Taken together these photographs of DCPD and its changed forms show that specific concentrations of zinc can (1) reduce the quantity of DCPD formed and (2) elicit the formation of less structured spherical forms that may be more soluble and therefore more easily removed if adhered to the enamel surface.

Anti-Tartar Clinical Study

A randomized, double-blind, parallel design study was performed to determine the anti-tartar efficacy of using the mouthwash composition of the present invention.

First, tests were performed to identify subjects that readily formed calculus. Each subject was given a complete prophylaxis to remove calculus. Each was instructed to brush twice daily with regular Crest® toothpaste for two months. Then each subject was scored for tartar using the Volpe-Manhold calculus index. The subjects were selected because of their ability to form tartar. A score of 7 or greater insured selection into phase two of the study.

In the next phase of the study the qualified subjects were given a professional cleaning and then given both a toothpaste and a mouthrinse to use. The first use of each was monitored to insure correct use. The subjects were instructed to brush for one minute and rinse with 20 ml of mouthwash for 30 seconds, twice daily. The subjects were also told to not eat, rinse or drink for 30 minutes afterwards. The subjects were visited after 6 weeks to examine compliance. Finally, after 12 weeks the subjects were measured for tartar and compliance was determined.

The four treatment groups were 1) a mouthrinse within the scope of the present invention that contained 0.09% zinc chloride and 0.064% thymol and regular Crest® toothpaste, 2) a mouthrinse within the scope of the present invention that contained 0.15% zinc chloride and 0.064% thymol and regular Crest® toothpaste, 3) a placebo mouthrinse and regular Crest® toothpaste and 4) a placebo rinse and tartar control Crest® toothpaste.

The results are summarized in Table 6. Both mouthrinses with zinc reduced the amount of tartar. The mouthrinse with 0.09% zinc reduced tartar by a higher percentage than Crest® Tartar Control toothpaste.

TABLE 6

	Placebo Rinse and Crest® Regular	0.09% Zinc Rinse and Crest® Regular	0.15% Zinc Rinse and Crest® Regular	Placebo Rinse and Crest® Tartar Control
Adjusted mean	9.68	7.92	8.26	8.09
p (vs. Placebo)		0.002	0.012	0.004
Reduction vs. Placebo		1.76	1.42	1.60
% Reduction vs. Placebo		18.2%	14.7%	16.5%

REDUCED ORAL MALODOR STUDIES

The presence of a zinc salt in a mouthwash composition greatly reduces oral malodor. This has been shown by measuring the cysteine VSC response, hedonic methodology and using a halimeter.

Cysteine VSC Response Study

Cysteine VSC response is measured using a halimeter. The subject rinses with 5 ml of 6 mM of Cysteine rinse or the subject mouthwash for thirty seconds at 20 minute intervals. The halimeter measures the amount of volatile sulfur compounds (VSC) in ppm of H_2S. Each graph represents the results from one subject.

Fig. 10 shows the cysteine VSC response rinsing with a control mouthwash without any zinc. Fig. 11 shows the cysteine VSC response rinsing with Formula 7. Fig. 12 shows the cysteine VSC response rinsing with Formula 8. The amount of zinc sulphate added is higher than zinc chloride to provide approximately equal amounts of zinc ions. Fig. 13 shows the cysteine VSC response of rinsing with Viadent®, which the inventors believe has approximately 0.2% $ZnCl_2$. The formulas used in this study are summarized in Table 7.

Control and Test Formulas

Stock solutions was prepared as follows. The units are grams except as noted.

	STOCK 1	STOCK 2
Alcohol.	864 ml	648 ml
Thymol	2.5569	1.918
Menthol	1.7038	1.2765
Eucalyptol	3.6937	2.9069
Methyl salicylate	2.6482	2.0087
1-Propanol	20.0117	15.030
Benzoic Acid	4.8090	3.602
Sodium Benzoate	1.4163	1.0686
Poloxamer 407	6.0073	6.0033
Water	qs to 1 liter	qs to 1 liter

The ingredients were mixed.

A second stock solution was made as follows:

	STOCK 3	STOCK 4
Seventy percent Sorbitol Solution	800.47	600.22
Caramel	0.9466	.07071
Water	qs to 1 liter	qs to 1 liter

The ingredients are mixed.

Mouthwash formulas based on one liter were made as follows:

TABLE 7

	CONTROL A	CONTROL B	FORMULA 7	FORMULA 8
STOCK 1	250 ml		250 ml	
STOCK 2		300 ml		300 ml
STOCK 3	250 ml		250ml	
STOCK 4		300 ml		300 ml
$ZnCl_2$			1.0042 gm	
$ZnSO_4$				2.1006 gms
Water	qs to 1000 ml	qs to 1000 ml	qs to 1000 ml	qs to 1000 ml

The cysteine VSC response graphs show that rinsing with control mouthwashes without zinc does not provide extended breath protection. Mouthwash formulas with zinc ions including as low as 0.1% $ZnCl_2$ or 0.21% $ZnSO_4$ provide significant breath protection that is comparable to a commercial mouthwash with twice as much $ZnCl_2$.

Hedonic Malodor Studies

Two studies were performed to test the breath freshening capacity of the present invention using either a hedonic scale or a halimeter. The mouthwash composition according to the present invention were tested against either a water control or a mouthwash outside the scope of the present invention. Formula 9 has 0.09% zinc chloride. Formula 10 has 0.15% zinc chloride. Control Formula C has no zinc salt. These formulas are summarized in Table 8. All numbers are in grams except as noted.

TABLE 8

INGREDIENT	FORMULA 9	FORMULA 10	CONTROL C
ALCOHOL U.S.P.	227 ml	227 ml	284 ml
THYMOL	.639	.639	.639
MENTHOL	.378	.378	.425
METHYL SALICYLATE	.66	.66	.66
EUCALYPTOL	.922	.922	.922
BENZOIC ACID	1.05	1.05	1.2
SODIUM BENZOATE	.503	.503	.354
POLOXAMER 407	2.5	2.5	1
CARAMEL			.236
MENTHYL SUCCINATE	.3	.3	
N-Ethyl-4 menthone-3-carboxamide	.05	.05	
MINT FLAVOR *	.25	.25	
ZINC CHLORIDE	.9	1.5	
1-PROPANOL	5	5	
SODIUM SACCHARIN, SPRAY DRIED	.3	.3	
SORBITOL SOLUTION	200	200	
WATER	QS TO 1 LITER	QS TO 1 LITER	QS TO 1 LITER

* The total menthol in Formulas 9 and 10 is .425 gm/ltr. The mint flavor contributes the remainder of the menthol.

Hedonic Test 1

The purpose of this test was to measure the overnight efficacy in reducing and controlling intrinsic oral malodor using hedonic methodology. The test was an observer-blind, parallel design using 99 subjects. The baseline hedonic odor rating (1=most pleasant...5=neutral...9=most objectionable) was measured on day 0 in the morning (7:00-8:30AM), the morning after a single use the previous evening (10:00-11:30PM) on day 0 with either Formula 9, Formula 10 or water control and the morning after two additional days of twice daily usage (7:00-8:30AM and 10:00-11:30PM). Post treatment hedonic rating were taken on day 1, 9 hours after a single use (in morning) and on Day 4 after 5 uses (in morning).

Both Formulas 9 and 10 were significantly superior ($p \leq 0.036$) to water control on Day 1 and Day 4. Formula 9 was not significantly different ($p \geq 0.521$) from Formula 4. The adjusted hedonic ratings are summarized in Table 9. The adjusted hedonic ratings are adjusted with respect to the baseline hedonic readings.

TABLE 9

Adjusted Hedonic Ratings

Treatment group	Time Period	
	Day 1 (overnight)	Day 4 (overnight)
Formula 9	6.88 *, **	6.94 *, **
Formula 10	6.77 *	6.90 *
Water Control	7.29	7.37

* significantly different from control ($p \leq 0.036$)

** Formula 9 not significantly different ($p \geq 0.521$) from Formula 10

Hedonic Test 2

This test was an observer-blind, parallel design study using 166 subjects. A baseline hedonic odor rating (1=most pleasant...5=neutral...9=most objectionable) was taken on day 0 in morning. Each subject used a mouthrinse and post-treatment hedonic ratings were taken at 30, 60, and 90 minutes and at 2, 3, 4, and 5 hours.

Formulas 9 and 10 are significantly superior ($p<0.001$) to water control at all time intervals from 30 minutes through 5 hours. Control C was significantly superior ($p \leq 0.016$) to water at 30, 60, and 90 minutes and 2, 3 and 5 hours. Formulas 9 and 10

were significantly superior ($p \leq 0.012$) to Control C at all times through 4 hours. The adjusted hedonic ratings are summarized in Table 10.

TABLE 10

Adjusted Hedonic Ratings:

Treatment	Time Period						
	30 min.	60 min	90 min	2 hours	3 hours	4 hours	5 hours
Formula 9	4.05 *, **	4.96*, **	5.48*, **	5.69*, **	5.97*, **	6.11*, **	6.31*
Formula 10	4.01*, **	5.06*, **	5.50*, **	5.78*, **	6.00*, **	6.24*, **	6.38*
Control C	4.53	5.66*	5.97*	6.10*	6.30*	6.55	6.51*
Water control	6.07	6.22	6.39	6.49	6.59	6.75	6.86

* significantly different ($p \leq 0.016$) from Water control
** significantly different ($p \leq 0.012$) from Control C

Halimeter Test

The overnight and long term efficacy of mouthrinses in reducing and controlling intrinsic oral malodor with daily use using a halimeter was measured. The test used a observer-blind, parallel design with 47 subjects. A baseline halimeter reading was taken on day 0 in the morning, the subjects rinsed with a single use in the evening on day 0 and then used the mouthrinse twice daily usage for 28 days. Post-treatment halimeter reading were taken on day 1 after a single 9 hour use (in morning), on day 7 after 13 uses (in morning) and on day 28 after 55 uses (in morning).

Both Formulas 9 and 10 are significantly superior ($p \leq 0.030$) to water control on Day 1, Day 7, and Day 28. Formula 9 not significantly different ($p \geq 0.318$) from Formula 10. The results are summarized in Table 11.

TABLE 11

Adjusted mean Halimeter VSC scores as ppb Sulfur:

Treatment group	Time Period		
	Day 1	Day 7	Day 28
Formula 9	106.89*, **	115.96*, **	112.57*, **
Formula 10	108.69 *	103.40 *	98.07*
Water Control	165.00	173.45	153.23

* significantly different from control ($p \leq 0.030$)

** Formulas 3 and 4 are not significantly different ($p \geq 0.318$)

TASTE TESTING

One advantage of the compositions according to the present invention is that they contain at least two ingredients that are known to taste bad, thymol and zinc salt, yet they provide superior taste. A taste test was performed using Formula 11, which contains 0.09% zinc chloride and 0.0639% thymol, Lavoris® Peppermint Mouthwash with 0.09% zinc chloride added and Lavoris® Peppermint Mouthwash with 0.09% zinc chloride and 0.0639 % thymol added.

Twenty three people were given randomly coded samples of each mouthwash and asked to rinse with each and chose which had the preferable taste. Eighteen chose Formula 11, five chose Lavoris® with 0.09% zinc chloride added and none choose Lavoris® with both 0.09% zinc chloride and 0.0639% thymol added.

Formula 11 (all units are grams except as noted)

Alcohol U.S.P.	227 ml
Menthol	0.425
Methyl Salicylate	0.66
Eucalyptol	0.922
Thymol	0.639
Mint Flavor	0.25
1-Propanol	5.0
Poloxamer 407	2.5
Sodium Benzoate	0.53
Benzoic Acid	1.05
Sodium Saccharin, granular	1.17
Zinc Chloride	0.9
70% Sorbitol Solution	200
FD&C Blue No. 1	0.006
Water	QS to 1 Liter

Other variations and modifications of this invention will be obvious to those skilled in this act. This invention is not limited except as set forth in the following claims.

WHAT IS CLAIMED IS:

1. An oral composition comprising:

thymol,

zinc ion in an amount from about 0.005 to about 0.095% by weight of the composition,

a sweetener; and

an aqueous vehicle.

2. The oral composition according to claim 1, wherein thymol is present in an amount from not more than about 0.1% by weight of the composition.

3. The oral composition according to claim 2, wherein thymol is present in an amount from about 0.02 to about 0.1% by weight of the composition.

4. The oral composition according to claim 3, wherein thymol is present in an amount from about 0.05 to about 0.075% by weight of the composition.

5. The oral composition according to claim 1, wherein the zinc ion is present in the composition by adding a zinc salt selected from the group consisting of zinc oxide, zinc stearate, zinc tribromosalicylanilide, zinc methionine sulfate, zinc carbonate, zinc tannate, zinc caprylate, zinc octoate, zinc oleate, zinc laurate, zinc silicate, zinc fluoride, zinc acetate, zinc formate, zinc lactate, zinc succinate, zinc fumarate, zinc iodide, zinc ammonium sulfate, zinc nitrate, zinc bromide, zinc phenol sulfonate, zinc chloride, zinc salicylate, zinc chromate, zinc sulfate, zinc citrate, zinc gluconate, zinc dithionate, zinc succinate, zinc fluorosilicate, zinc glycerophosphate, zinc tartarate and mixtures thereof.

6. The oral composition according to claim 5, wherein the zinc salt is selected from the group consisting of zinc chloride, zinc citrate, zinc oxide, zinc acetate, zinc stearate, zinc methionine sulfate, zinc phenol sulfonate, zinc sulfate, and zinc gluconate.

7. The oral composition according to claim 6, wherein the zinc salt is zinc chloride.

8. The oral composition according to claim 1, wherein the sweetener is selected from the group consisting of sodium saccharin, calcium saccharin, cyclamate salts, the sodium, ammonium or calcium salts of 3,4-dihydro-6-methyl-1,2,3-oxathiazine-4-one-2,2-dioxide, the potassium salt of 3,4-dihydro-6-methyl-1,2,3-oxathiazine-4-one-2,2-dioxide, the free acid form of saccharin, aspartame, and mixtures thereof.

9. The oral composition according to claim 8, wherein the sweetener is sodium saccharin.

10. The oral composition according to claim 1, further comprising eucalyptol, menthol and methyl salicylate.

11. The oral composition according to claim 10, wherein the eucalyptol is present in an amount from about 0.07 to about 0.11% by weight, the menthol is present in an amount from about 0.03% to about 0.06% by weight and the methyl salicylate is present in an amount from about 0.03 to about 0.08% by weight.

12. The oral composition according to claim 11, wherein the eucalyptol is present in an amount from about 0.08 to about 0.10% by weight, the menthol is present in an amount from about 0.04 to about 0.05% by weight and the methyl salicylate is present in an amount from about 0.04 to about 0.07% by weight.

13. A method for inhibiting tartar in an oral cavity comprising introducing to the oral cavity an oral composition comprising:

thymol,

zinc ion in an amount from about 0.005 to about 0.095% by weight of the composition,

a sweetener; and

an aqueous vehicle.

14. The method according to claim 13, wherein thymol is present in an amount from not more than about 0.1% by weight of the composition.

15. The method according to claim 14, wherein thymol is present in an amount from about 0.02 to about 0.1% by weight of the composition.

16. The method according to claim 15, wherein thymol is present in an amount from about 0.05 to about 0.075% by weight of the composition.

17. The method according to claim 13, wherein the zinc ion is present in the composition by adding a zinc salt selected from the group consisting of zinc oxide, zinc stearate, zinc tribromosalicylanilide, zinc methionine sulfate, zinc carbonate, zinc tannate, zinc caprylate, zinc octoate, zinc oleate, zinc laurate, zinc silicate, zinc fluoride, zinc acetate, zinc formate, zinc lactate, zinc succinate, zinc fumarate, zinc iodide, zinc ammonium sulfate, zinc nitrate, zinc bromide, zinc phenol sulfonate, zinc chloride, zinc

salicylate, zinc chromate, zinc sulfate, zinc citrate, zinc gluconate, zinc dithionate, zinc succinate, zinc fluorosilicate, zinc glycerophosphate, zinc tartarate and mixtures thereof.

18. The method according to claim 17, wherein the zinc salt is selected from the group consisting of zinc chloride, zinc citrate, zinc oxide, zinc acetate, zinc stearate, zinc methionine sulfate, zinc phenol sulfonate, zinc sulfate, and zinc gluconate.

19. The method according to claim 18, wherein the zinc salt is zinc chloride.

20. The method according to claim 13, wherein the sweetener is selected from the group consisting of sodium saccharin, calcium saccharin, cyclamate salts, the sodium, ammonium or calcium salts of 3,4-dihydro-6-methyl-1,2,3-oxathiazine-4-one-2,2-dioxide, the potassium salt of 3,4-dihydro-6-methyl-1,2,3-oxathiazine-4-one-2,2-dioxide, the free acid form of saccharin, aspartame, and mixtures thereof.

21. The method according to claim 20, wherein the sweetener is sodium saccharin.

22. The method according to claim 13, further comprising eucalyptol, menthol and methyl salicylate.

23. The method according to claim 22, wherein the eucalyptol is present in an amount from about 0.07 to about 0.11% by weight, the menthol is present in an amount from about 0.03% to about 0.06% by weight and the methyl salicylate is present in an amount from about 0.03 to about 0.08% by weight.

24. The method according to claim 23, wherein the eucalyptol is present in an amount from about 0.08 to about 0.10% by weight, the menthol is present in an amount from about 0.04 to about 0.05% by weight and the methyl salicylate is present in an amount from about 0.04 to about 0.07% by weight.

25. A method for making an oral composition comprising mixing the following ingredients:

thymol,

a zinc salt in an amount sufficient to provide zinc ion in an amount from about 0.005 to about 0.095% by weight of the composition,

a sweetener; and

an aqueous vehicle.

26. The method according to claim 25, wherein thymol is present in an amount from not more than about 0.1% by weight of the composition.

27. The method according to claim 26, wherein thymol is present in an amount from about 0.02 to about 0.1% by weight of the composition.

28. The method according to claim 27, wherein thymol is present in an amount from about 0.05 to about 0.075% by weight of the composition.

29. The method according to claim 25, wherein the zinc salt is selected from the group consisting of zinc oxide, zinc stearate, zinc tribromosalicylanilide, zinc methionine sulfate, zinc carbonate, zinc tannate, zinc caprylate, zinc octoate, zinc oleate, zinc laurate, zinc silicate, zinc fluoride, zinc acetate, zinc formate, zinc lactate, zinc succinate, zinc fumarate, zinc iodide, zinc ammonium sulfate, zinc nitrate, zinc bromide, zinc phenol sulfonate, zinc chloride, zinc salicylate, zinc chromate, zinc sulfate, zinc citrate, zinc gluconate, zinc dithionate, zinc succinate, zinc fluorosilicate, zinc glycerophosphate, zinc tartarate and mixtures thereof.

30. The method according to claim 29, wherein the zinc salt is selected from the group consisting of zinc chloride, zinc citrate, zinc oxide, zinc acetate, zinc stearate, zinc methionine sulfate, zinc phenol sulfonate, zinc sulfate, and zinc gluconate.

31. The method according to claim 30, wherein the zinc salt is zinc chloride.

32. The method according to claim 25, wherein the sweetener is selected from the group consisting of sodium saccharin, calcium saccharin, cyclamate salts, the sodium, ammonium or calcium salts of 3,4-dihydro-6-methyl-1,2,3-oxathiazine-4-one-2,2-dioxide, the potassium salt of 3,4-dihydro-6-methyl-1,2,3-oxathiazine-4-one-2,2-dioxide, the free acid form of saccharin, aspartame, and mixtures thereof.

33. The method according to claim 32, wherein the sweetener is sodium saccharin.

34. The method according to claim 25, further comprising eucalyptol, menthol and methyl salicylate.

35. The method according to claim 34, wherein the eucalyptol is present in an amount from about 0.07 to about 0.11% by weight, the menthol is present in an amount from about 0.03% to about 0.06% by weight and the methyl salicylate is present in an amount from about 0.03 to about 0.08% by weight.

36. The method according to claim 35 wherein the eucalyptol is present in an amount from about 0.08 to about 0.10% by weight, the menthol is present in an amount from

about 0.04 to about 0.05% by weight and the methyl salicylate is present in an amount from about 0.04 to about 0.07% by weight.

FIG-1 EFFECT OF Zn ON INDUCTION TIME
3.0 mL

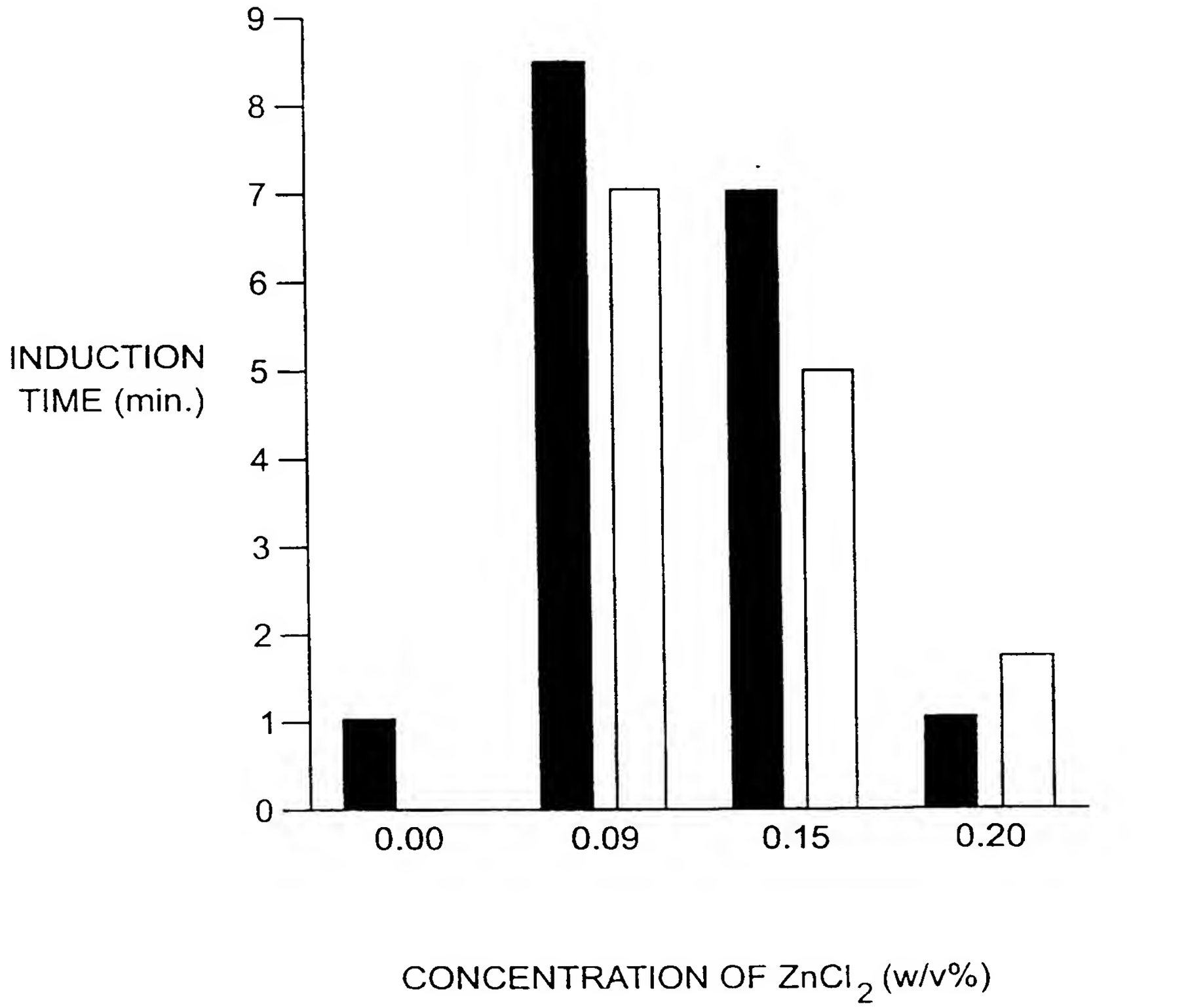


FIG-2 EFFECT OF Zn ON INDUCTION TIME
1.5 mL

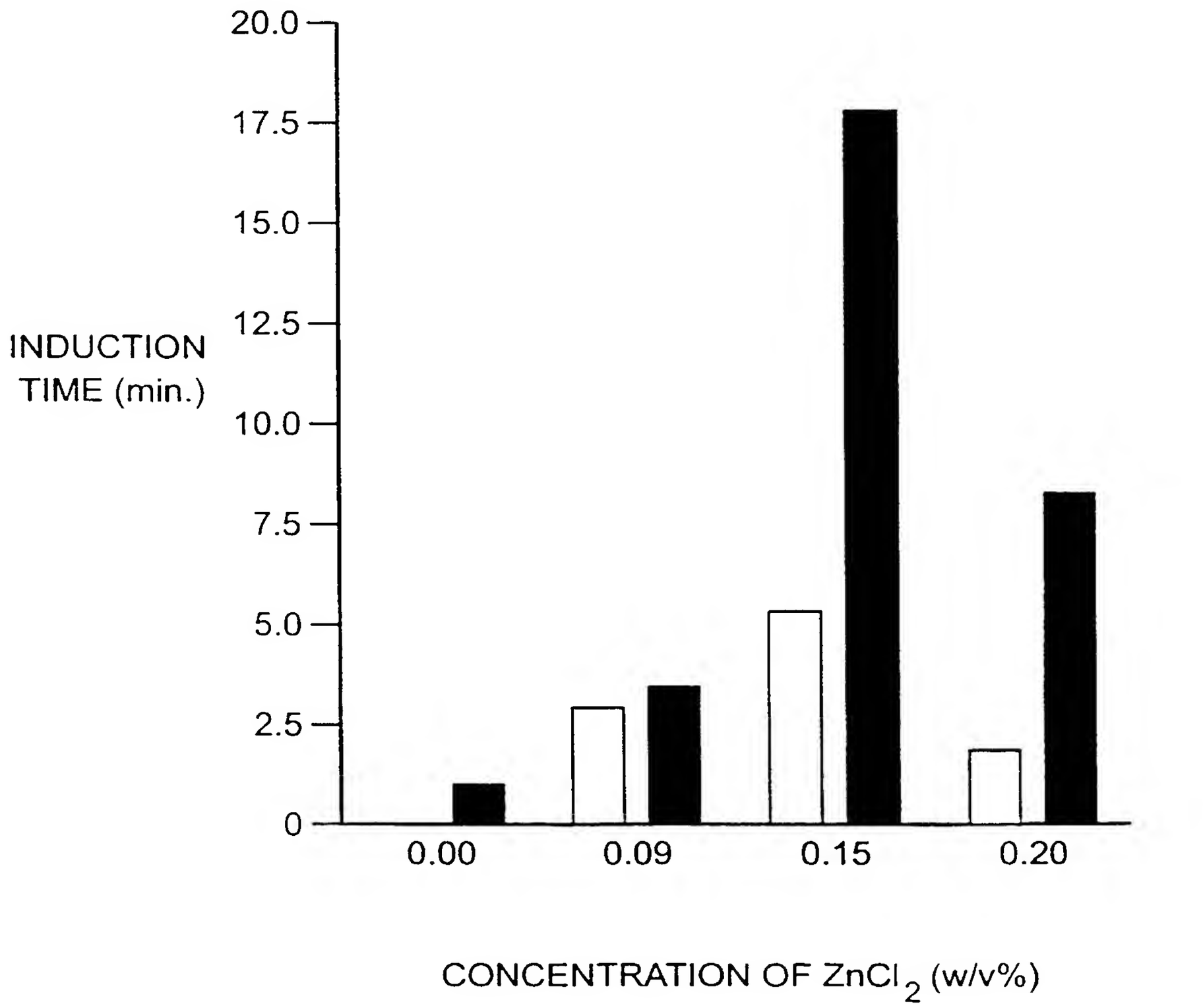


FIG-3 EFFECT OF Zn ON INDUCTION TIME
1.5 mL

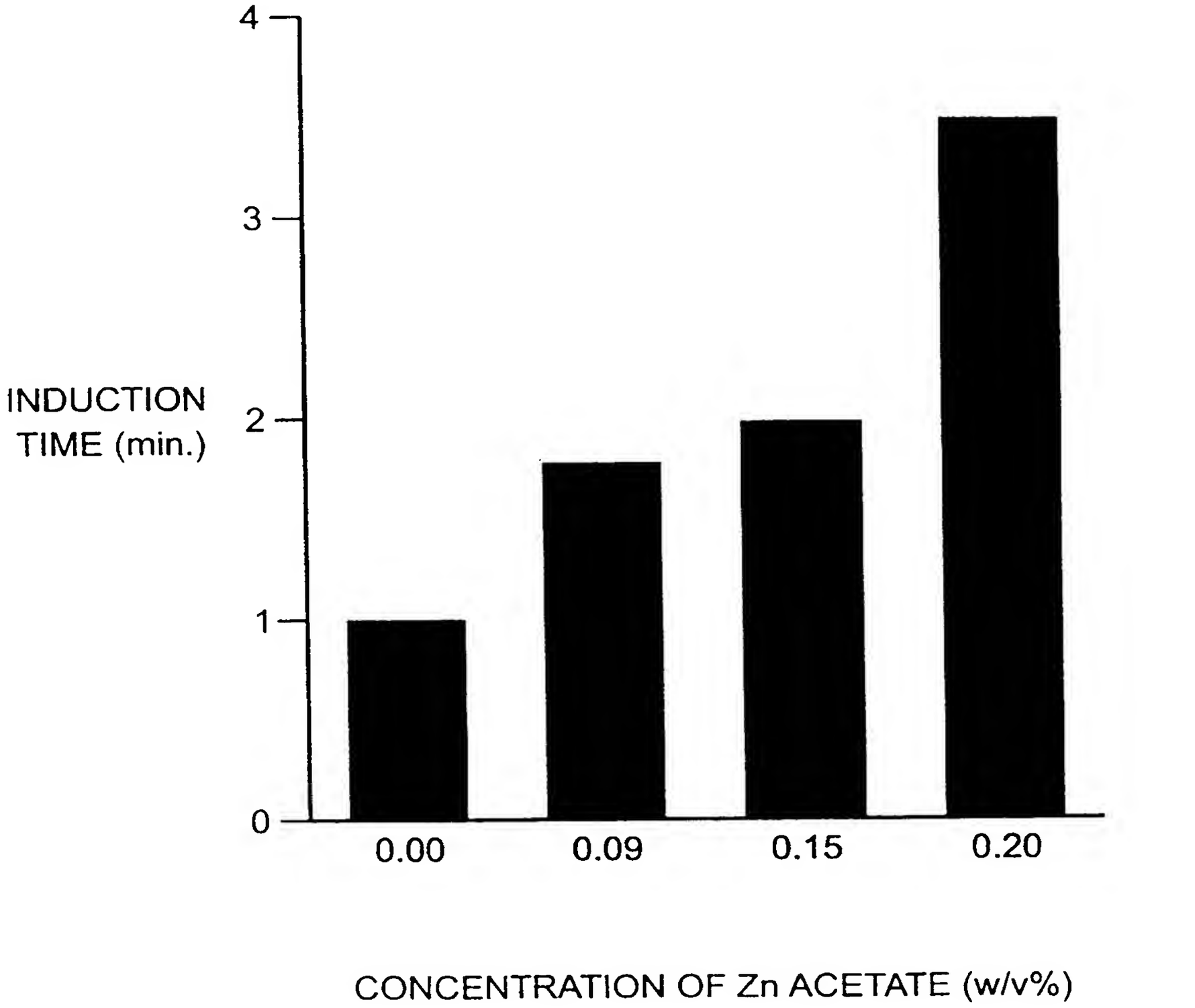


FIG-4

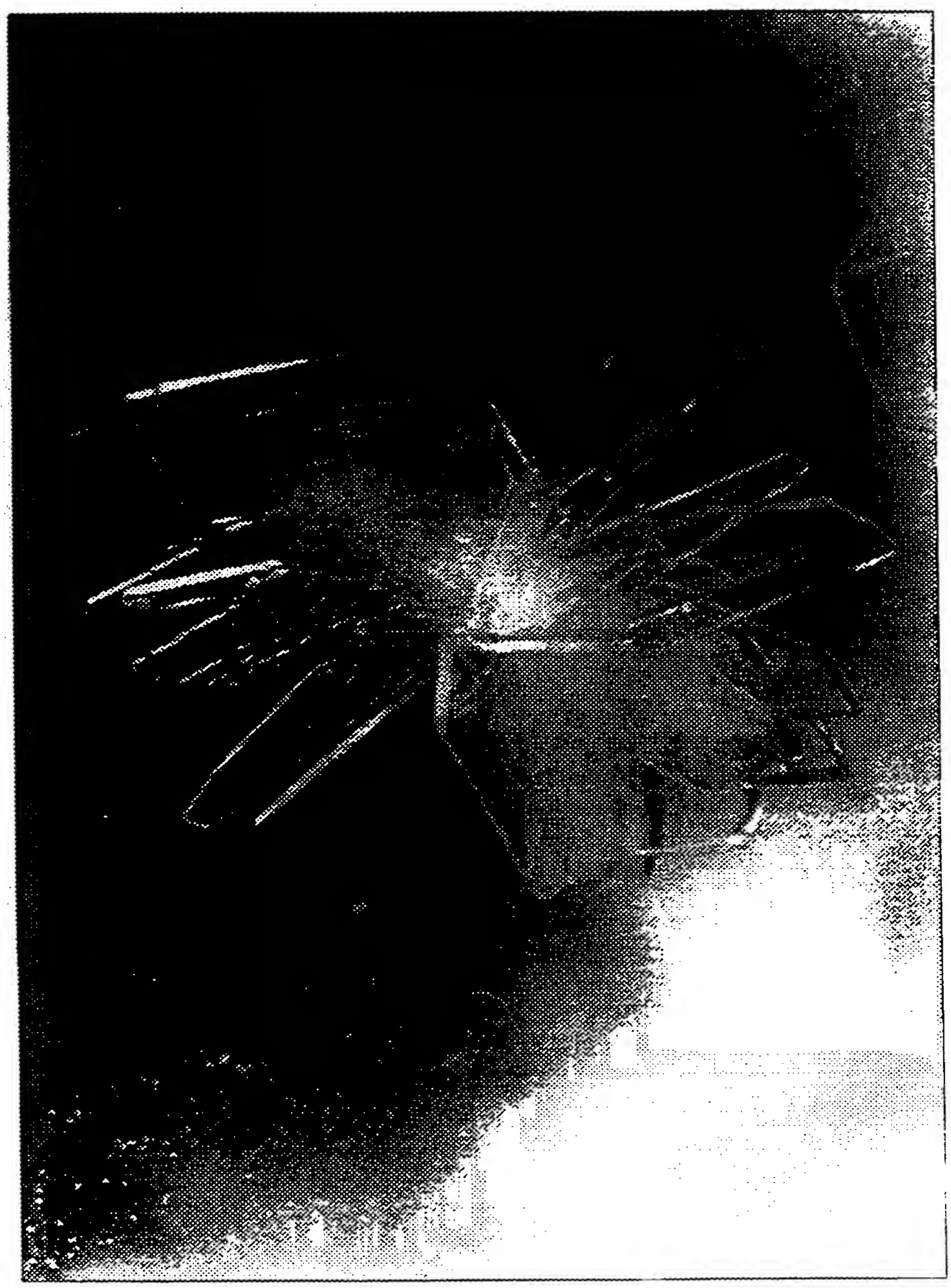


FIG-5

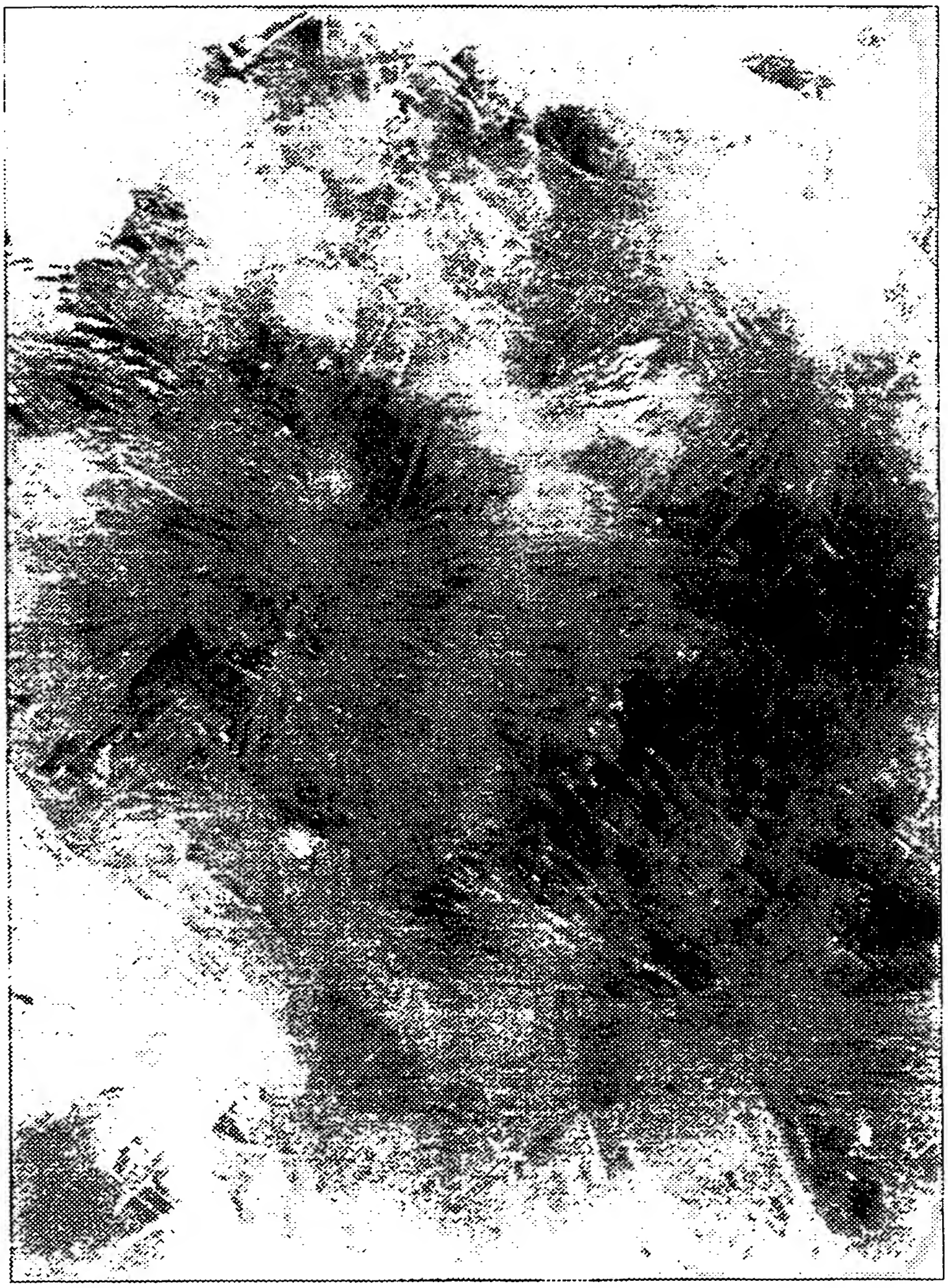


FIG-6

FIG-7

FIG-8

FIG-9

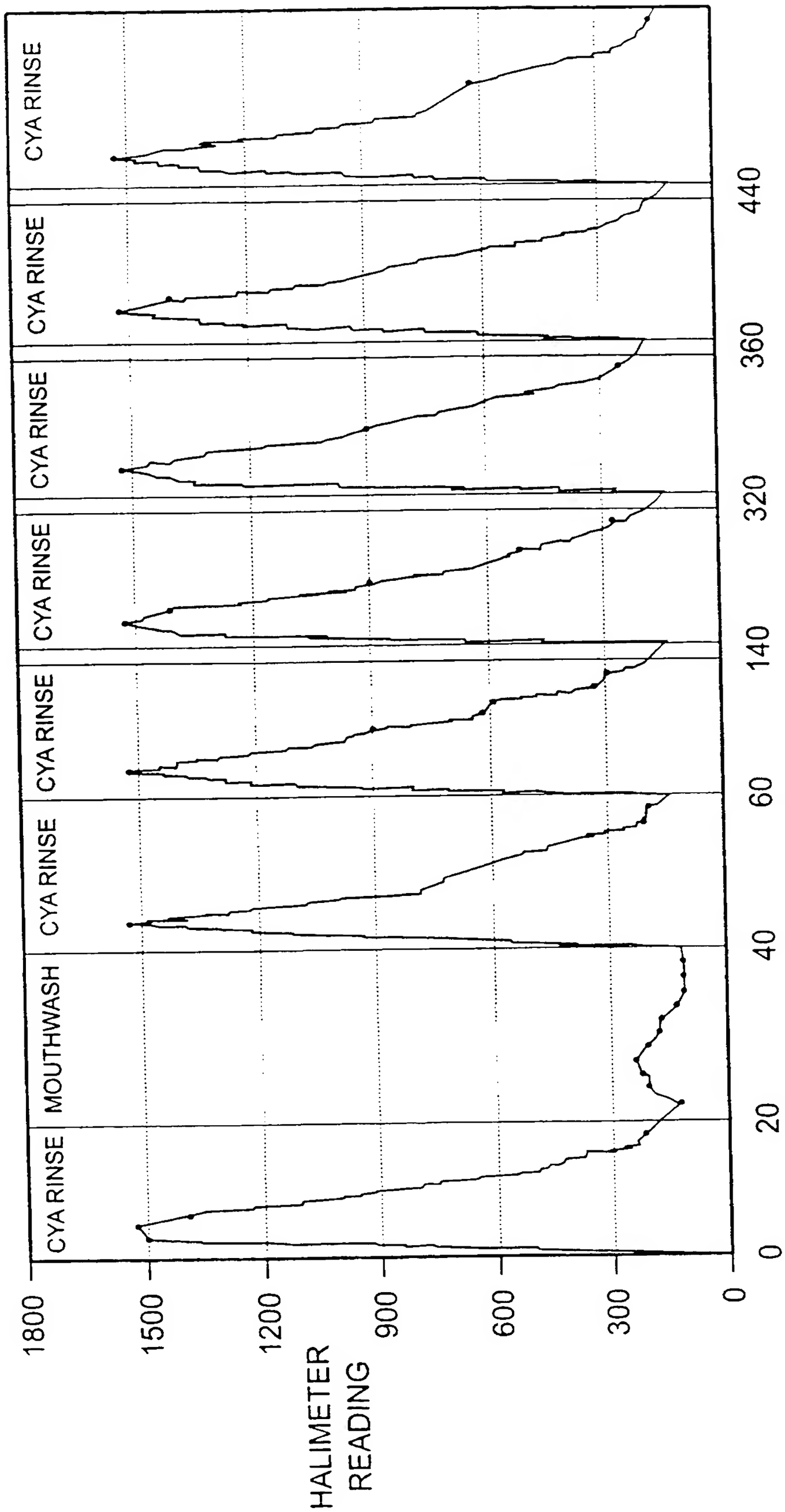


FIG-10 EFFECT OF RINSING WITH MOUTHWASH PROTOTYPE ON THE CYSTEINE VSC RESPONSE

FIG-11 EFFECT OF RINSING WITH MOUTHWASH PROTOTYPE CONTAINING 0.1% $ZnCl_2$ ON THE CYSTEINE VSC RESPONSE

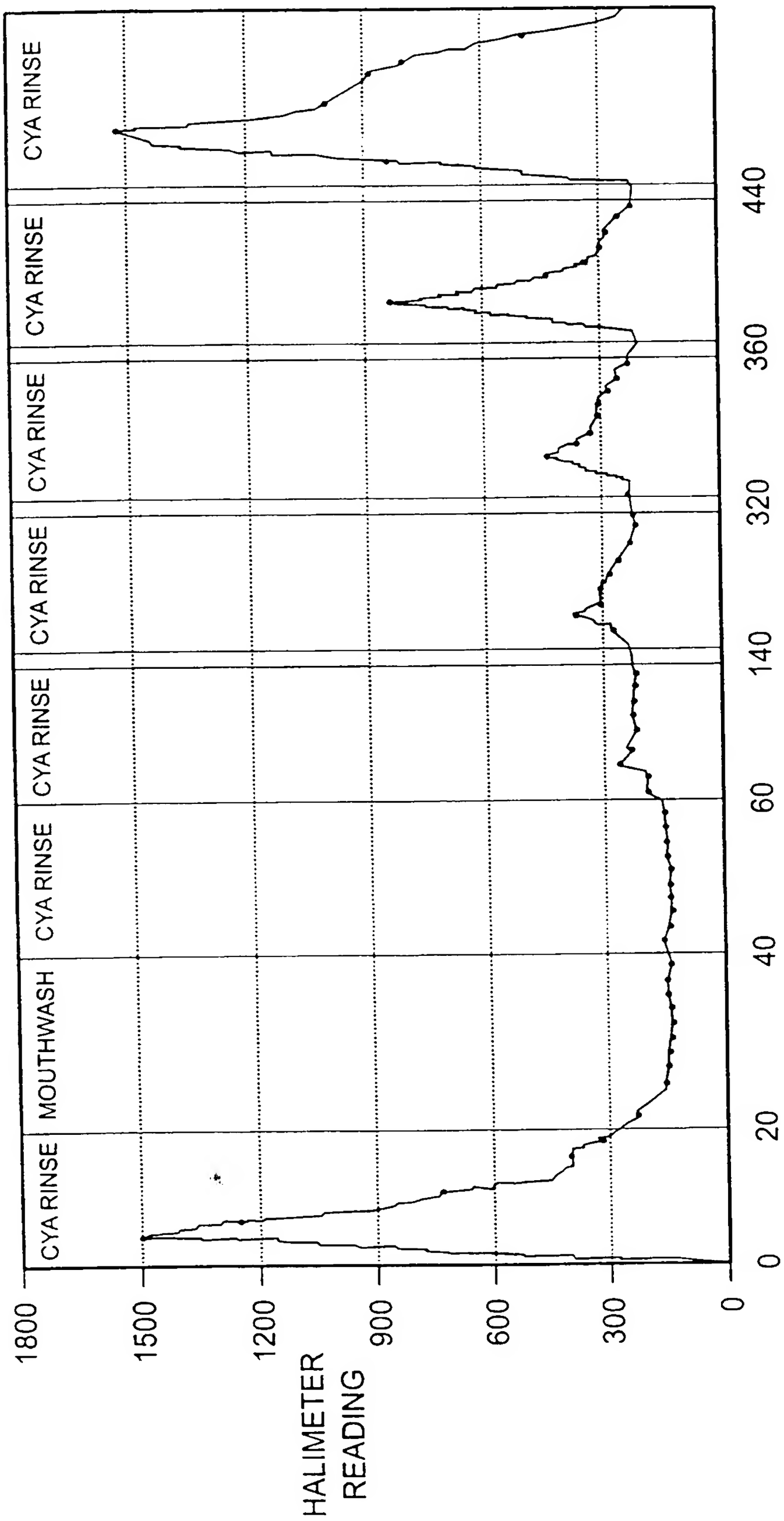


FIG-12 EFFECT OF RINSING WITH MOUTHWASH PROTOTYPE CONTAINING 0.21% $ZnSO_4$ ON THE CYSTEINE VSC RESPONSE

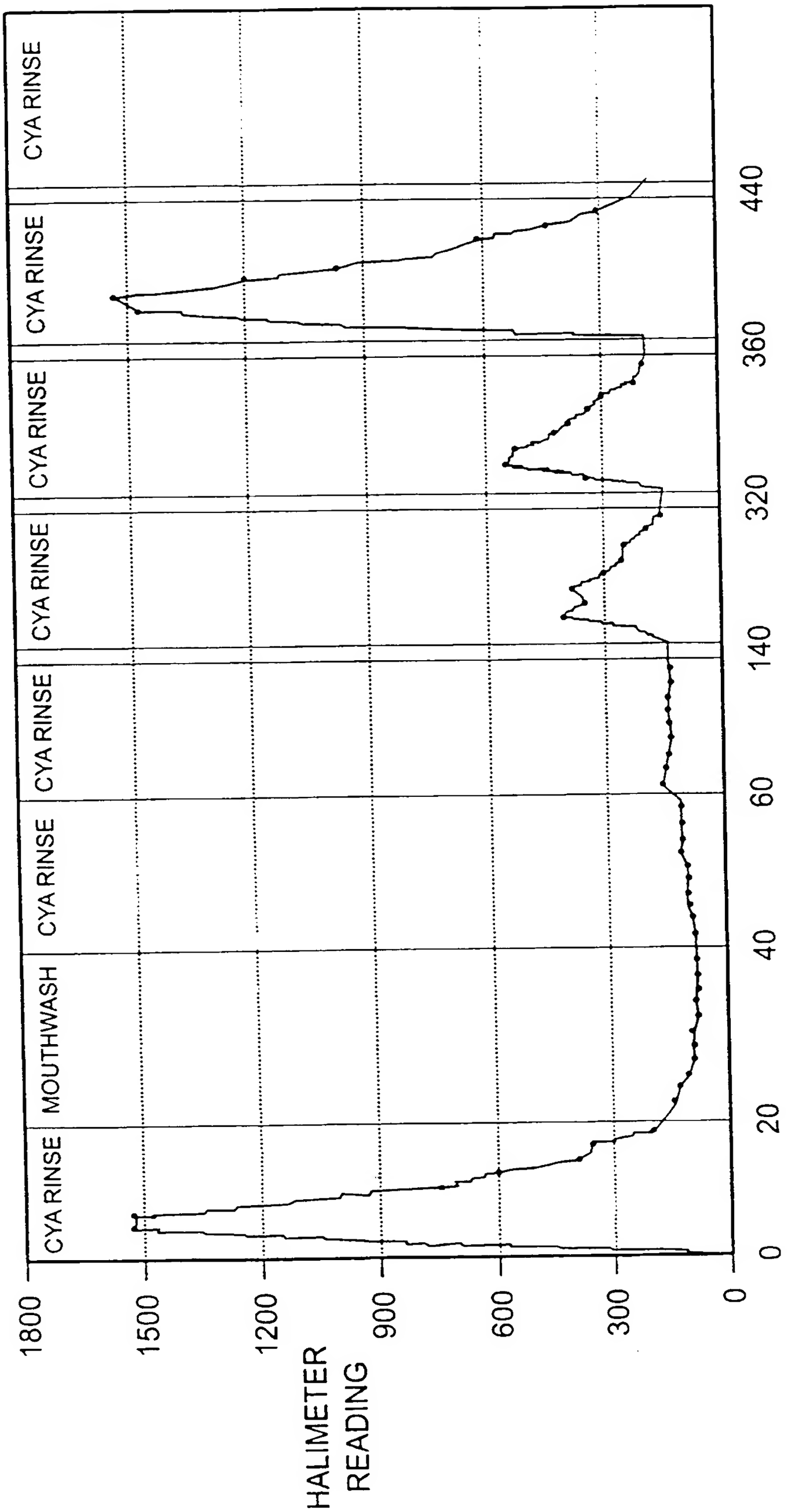
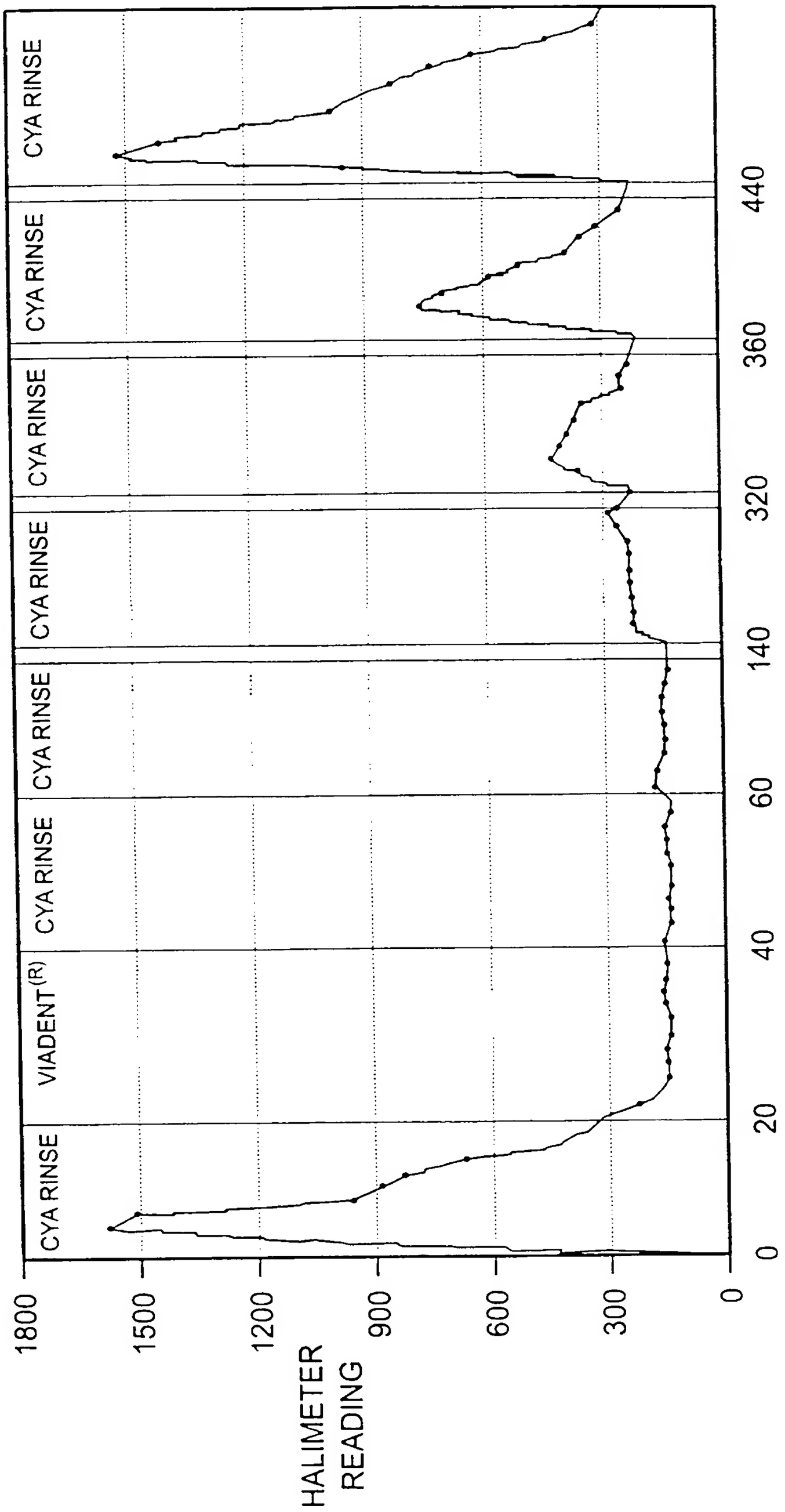


FIG-13 EFFECT OF RINSING WITH VIADENT$^{(R)}$ (0.2% $ZnCl_2$) ON THE CYSTEINE VSC RESPONSE



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(57) Abstract

An oral composition that includes thymol, a zinc salt and a sweetener is disclosed. The oral composition has antitartar, antiplaque, antigingivitis efficacy, long lasting breath freshening and high consumer acceptability in spite of the presence of two ingredients, thymol and a zinc salt, that are known to taste bad.

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 99/09135

A. CLASSIFICATION OF SUBJECT MATTER

A 61 K 7/16, A 61 K 33/30

According to International Patent Classification (IPC) or to both national classification and IPC6

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Minimum documentation searched (classification system followed by classification symbols)

A 61 K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 97/40812 A1 (WARNER-LAMBERT COMPANY) 06 November 1997, pages 3-6, page 7, lines 19-23. --	1-12
A	WO 96/11694 A2 (GOMBERT, B.) 25 April 1996, claims. ----	1-12

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